Patent
Attorney's Docket No. 0070777-000014

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Ju-Ock NAM et al.	)	Group Art Unit: 1654
	)	
Application No.: 10/552,291	)	Examiner: Christina Bradley
	)	
Filed: October 3, 2005	)	Confirmation No.: 6194
	)	
For: USE OF A PEPTIDE THAT INTERACTS WITH ALPHA V BETA 3 INTEGRIN OF ENDOTHELIAL CELL	)	

DECLARATION OF DR. YOUNG MO KANG

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. I, Dr. Young Mo Kang, declare the following:

2. I am a citizen of the Republic of Korea, and have the following mailing address: Cell and Matrix Biology National Research Laboratory; Department of Biochemistry, Kyungpook National University School of Medicine, 101 Dongin-Dong, Jung-gu, Daegu, 700-422, Republic of Korea;

3. I graduated from Kyungpook National University School of Medicine with M.D. and a Ph.D. degrees in 1996;

4. I am a professor in the Department of Biochemisty of Kyungpook National University School and a clinical instructor in the Department of Internal Medicine (Rheumatism);

5. I have read and am familiar with the above-identified United States patent application filed October 3, 2004, and I am submitting this Declaration in support of that application;

6. I have performed and/or supervised the experiments reported below:

Object

The inventors of the above-identified application have determined that βig-h3 controls the function of the synoviocytes that play an important role in arthritis. In particular, the inventors have discovered that βig-h3 is involved in the angiogenesis which is necessarily required for the generation of inflammation, and that the function of βig-h3 is due to interaction with the integrin that is expressed at the cell surface. In addition, the present inventors have shown that a βig-h3 derived peptide of the present invention (YH18) binds to integrin, controls the functions of synoviocytes, and suppresses angiogenesis. (See, e.g., page 11, paragraph 15 of the specification.) The results disclosed in the above-identified application show that the YH18 peptide can be used to treat arthritis. In the experiments set forth herein, the therapeutic effect of the YH18 peptide was further demonstrated in an arthritis animal model.

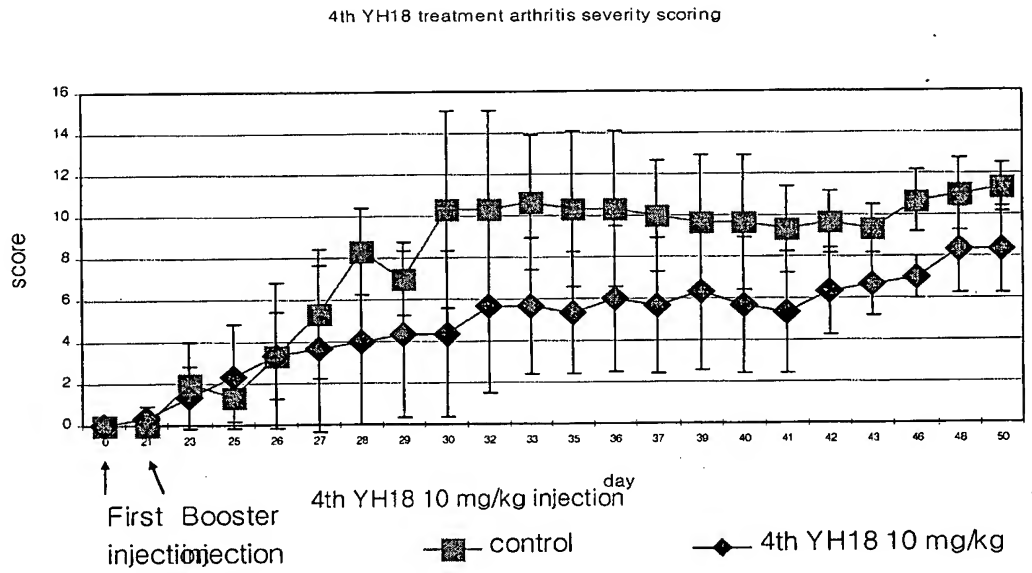
Method

The YH18 peptide was designed using an amino acid sequence that is located in the fourth fas-1 domain of the mouse βig-h3, and its synthesis was performed using a synthesizer. A mouse model of collagen-induced arthritis, which is the most clinically similar to human rheumatoid arthritis, was designed using type II collagen. More particularly, collagen-induced arthritis was induced by subcutaneously injecting native bovine type II collagen (100μg) into a DBA1/J mouse. After the secondary administration of the type II collagen, the YH18 peptide was intraperitoneally injected at a dose of 10 mg/kg at the time when the mouse developed the arthritis. Next, the intraperitoneal injection was repeated for 14 days. Severity of the arthritis was observed with the naked eye, and then evaluated as Severity Level 1 when mild edema appeared in one of four joints; Severity Level 2 when severe edema appeared in at lest two joints; Severity Level 3 when severe edema appeared in most of the joints; and Severity Level 4 when severe edema

appeared in the entire mouse legs. The results were quantitified as a clinical arthritis index. In order to observe the duration of the post-therapeutic effect, the clinical arthritis index was measured and calculated for a further 15 days.

Results

The results of the experiment show that treatment with the YH18 peptide effectively suppresses the severity of arthritis in a murine collagen-induced arthritis model. Furthermore, the suppressive effect on the arthritis lasted for 15 days (see the following drawing). These results indicate that the YH18 peptide is effective as a therapeutic agent to treat chronic arthritis such as rheumatoid arthritis.



7. The results detailed above demonstrate that a peptide according to the present invention can be used to treat arthritis in a well-accepted arthritis animal model;

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 2007. 6. 2

By: _____
Young Mo Kang